修士論文要旨

Relationship between Thermal Preference and Thermosensitive TRPs in Ovariectomized Mice

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Introduction. Female hormones are known to be associated with body temperature. The relationship between female hormone and thermal preference has been investigated. It is suggested that the thermoneutral zone, the range of temperature at which metabolic rate is maintained at lowest, of ovariectomized (OVX) rats is lower than that of OVX rats with estradiol replacement. However, it remains unclear whether female hormones affect thermal preference. Transient receptor potential (TRP) channels are cation channels found in 1989. Mammalian TRP channels are divided into seven subfamilies and six members are regarded as thermosensitive TRPs. TRPM8 is activated by innocuous cool temperatures (< 25° C) and menthol. TRPV1 known as a capsaicin receptor is also activated by heat (> 43° C). In recent years, the effect of estradiol on the thermosensitive TRPs has been examined. In the present study, I hypothesized that estradiol would affect the expression of TRPV1 and TRPM8; in consequence, thermal preference would be changed. The purpose of present study was verifying the hypothesis and building an experimental apparatus to evaluate thermal preference of mice.

Methods. Female ICR mice (n = 22, age of 9 w) were used in the present study. Mice underwent bilateral ovariectomy (the OVX group, n = 12) or sham operation (the sham group, n = 10). After recovery for a week, thermal preference tests were performed (the young-sham group, n = 6; the young-OVX group, n = 6) using the new experimental apparatus (Fig. 1). Each mouse was put in the apparatus, and could move freely in any area for 90 minutes. During the tests, one of the Peltier boards was set at 32℃ and other boards were set at 18℃ (cold trials) or 43 ℃ (hot trials). The setting of temperature was changed every 5 minutes. Each mouse conducted the cold trial and hot trial twice on a different day. The location of the mice was recorded every 10 seconds. The same tests were conducted for other mice groups, which had surgery 4 - 7 months before (the old-sham group, n = 4; the old-OVX group, n = 6). The expression of TRPV1 and TRPM8 were examined by immunofluorescence.

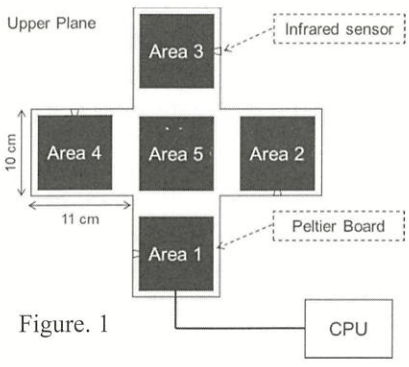

Figure. 1

Results. During first cold trial, the counts which mice chose the area at 32℃ were greater in the old-sham group than in the young-sham group (p = 0.008; the young-sham group, 108 ± 5 times; the old-sham group, 163 ± 13 times). The counts in the old-sham group were greater than those in the old-OVX group (p = 0.19; the old-OVX group, 116 ± 10 times). During the hot trials, there was no significant difference among the groups. The counts in every group were significantly greater during the first 30 minutes than during the last 30 minutes (first trial, p = 0.047; second trial, p = 0.007). The counts in every group were significantly greater during the second 30 minutes than during the last 30 minutes (first trial, p = 0.001; second trial, p = 0.003). The expression of TRPV1 and TRPM8 at the plantar skin tended to be greater in the young groups than in the old groups.

Discussion. During first cold trial of thermal preference tests, the counts of selecting 32℃ area were greater in the old-sham group than in the young-sham and the old-OVX groups. Previous study has shown that mice of 11 months old preferred nearly 2℃ warmer environment than mice of 2 months old. Some mice in the old groups were over 9 months old; thus, there was possibility that the old-sham group preferred warmer temperature affected by aging. The counts in the old-OVX group had a trend to be fewer than other groups during cold trials. Thermoneutral zone of OVX rats have been reported to shift lower than that of OVX rats with estradiol replacement. These observations suggest that the temperature mice feel comfortable might be decreased by long-term deficiency of estradiol. TRPV1 and TRPM8 at the plantar skin tended to express greater in the young groups than in the old groups. Cold sensitivity in the old groups might be reduced by lower expression of TRPM8, but the old-sham mice preferred 32℃ area more than the young-sham mice. Consequently, thermal preference might be regulated by mechanisms independent of thermal sensation. In conclusion, present study suggested that thermal preference might be changed by bilateral ovariectomy; however, thermosensitive TRPs at the skin might not affect the fluctuation.